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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,909	02/02/2001	Mark Roberts	M0975/7006 (JRV)	9660

7590 04/19/2004

John R. Van Amsterdam
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/775,909	ROBERTS, MARK	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,39 and 41-55* is/are pending in the application.

4a) Of the above claim(s) *47-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37, 39, 41-46 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1-8-04 has been entered.

Claims 37, 39, 41-46 and 55 are pending and under examination. Claims 47-54 are withdrawn from consideration.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

The rejections over the art of record are withdrawn in view of the specific amendment to the claims.

New Rejections

Claim Objections

Claim 43 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 37 requires that the method comprises co-administration of the adjuvant and antigen. The limitation of claim 43 recites that they are administered at the same time. Co-administration by definition is the administration at the same time and as such, this claim is not viewed as limiting claim 37 from which it depends.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37, 39, 41-46 and 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants indicate that the limitation that the antigen is not pertussis toxin can be found in the specification at page 1, first full paragraph, page 6 last full paragraph, page 7 4th-6th full paragraphs, page 8 the 3rd and 4th full paragraphs, and the paragraph bridging pages 9-10 and the first full paragraph on page 10. Applicants argue that the specification at page 1, contemplates antigens co-administered with the adjuvant composition and argues that this provides for conception that the pertussis toxin is not an antigen. This is not persuasive because there is no indication that the antigen is not pertussis toxin in this passage. The passage merely recites a combination of an adjuvant with an antigen and does not exclude pertussis toxin as the antigen. The specification clearly indicates that the pertussis toxin is also an antigen (page 6, third full paragraph) and therefore would

fall within the definition of an antigen. Pertussis toxin by nature of its specific structure innately has both properties of an antigen and an adjuvant. These properties are innate to the structure of the pertussis toxin of the art as demonstrated by the art of record. This specification does not contemplate by way of written description that the pertussis toxin can only function as an adjuvant, to the exclusion of its function as an antigen. These paragraphs do not contemplate such and the specification does not teach such. Applicants argue that because the claims require co-administration of the adjuvant and the antigen, and because if pertussis toxin were also the antigen, there would not be any need to co-administer an antigen and indicates that the last full paragraph of page 6 supports this conclusion. This is not persuasive, the specification clearly states any antigen in combination with the adjuvant (page 1, first paragraph). The specification does not exclude pertussis toxin as the antigen and clearly identifies it as such (page 6, third full paragraph). The now recited negative limitation of not pertussis toxin does not logically flow therefrom. The recitation in the positive of some antigens that are not pertussis toxin (pages 9-10), does not support exclusion of a particular antigen in the negative when all protective antigens are contemplated by the specification as filed and pertussis toxin/toxoid is a known protective antigen. Applicants attempt to mix and match independent concepts of the specification to derive the negative limitation. The teachings relied upon are general and specifically indicate that pertussis antigens can be co-administered (see relied upon passages at pages 9-10) and do not limit these antigens as not pertussis toxin, but any antigen. None of the passages of the specification teach nor contemplate that the co-administered antigen is not pertussis toxin and specifically states that any pertussis antigen can be employed (page 9-10). The specification teaches the same dosages for antigen and adjuvant effects and as such, it would be clear to one skill in the art that the adjuvant activity is not separable from the adjuvant activity and that Applicants at the time of filing had not contemplated the new subgenus of the co-administered antigen not being pertussis toxin from the recited passages.

Claims 37, 39, 41, 43, 44, 46 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al (Vaccine, 11(2):113-118, 1993; of record) in view of Nenconi et al (Acta Med Rom 29:78-83, 1991; of record).

Wilson et al teach that pertussis toxin was able to stimulate a response when fed in conjunction with keyhole limpet hemocyanin and that the adjuvant activity of pertussis toxin is a property of the enzymatically active A subunit (i.e. the instant S1). Wilson et al teach the role of the A subunit as an adjuvant appears independent of its ability to increase the activity of adenylate cyclase by means of ADP-ribosylating GTP-binding regulatory proteins, since a direct activator of adenylate cyclase had no effect on the mucosal response (see abstract). Wilson et al differ by not using a non-toxic double mutant or a protective antigen for oral feeding.

Nenconi et al teaches a non-toxic double mutant of pertussis toxin (PT-9K/129G) that abolishes the enzymatic activity of the S1 subunit and all the toxic properties of PT, without changing the immunological properties of the wild type toxin. Nenconi et al teach that the double mutant has been combined with other the protective antigens FHA and 69K of pertussis, diphtheria and tetanus toxoid for injection as a vaccine.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to administer the composition of the double mutant PT-9K/129G) in combination with the FHA, 69K pertussis protective antigens, diphtheria and tetanus toxoid by oral administration according to Wilson et al in order to generate a protective immune response in a mammal to FHA, 69K, diphtheria and tetanus toxoid antigens because Nenconi et al teaches that the double mutant (PT-9K/129G) retains all the immunological properties of the toxin without the toxic enzymatic activity and Wilson et al teach the adjuvant activity appears independent of the enzymatic activity of the S1 subunit and as such one skilled in the art would have reasonable expected at the time that

the invention was made that the modified S1 subunit would also have the adjuvant function of the native S1 toxin of the art.

Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al (Vaccine, 11(2):113-118, 1993; of record) and Nenconi et al (Acta Med Rom 29:78-83, 1991; of record) as applied to claims 37, 39, 41, 43, 44, 46 and 55 above and further in view of Capiau et al (EP 352250, published 1-24-90; of record) and Tamura et al (U.S. Patent No. 5,182,109; of record).

Wilson et al (Vaccine, 11(2):113-118, 1993) and Nenconi et al (Acta Med Rom 29:78-83, 1991) are combined as set forth supra. The references as combined do not teach intranasal administration of a vaccine composition.

Capiau et al teach methods or oral or intranasal vaccination using compositions comprising non-toxic mutants of pertussis in combination with non-pertussis toxin antigens, FHA, tetanus toxoid and/or diphtheria toxoid or any other protective antigen of Bordetella pertussis (see page 7, lines 50-56 and page 8, lines 41-59).

Tamura et al teach preparations comprising toxins such as pertussis toxin as an adjuvant in combination with vaccine agents can be administered intranasally in the form of a nasal spray or drops. Tamura et al teach that the nasal administration has the benefit of stimulating IgA antibody production (see column 3).

It would have been *prima facie* obvious to one having ordinary skill in the art to administer the preparation according to Wilson et al and Nenconi et al as combine supra according to the intranasal methods of Capiau et al and Tamura et al for the expected benefit of stimulating a protective IgA response to the non-toxin antigens in the vaccine composition one skilled in the art would have reasonable expected at the time that the invention was made that the modified S1 subunit would also have the adjuvant function of the native S1 toxin of the art because Wilson et al teach the double mutant (PT-9K/129G) retains all the immunological properties of the toxin without the toxic enzymatic activity

and Wilson et al teach the adjuvant activity appears independent of the enzymatic activity.

Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al (Vaccine, 11(2):113-118, 1993; of record) and Nenconi et al (Acta Med Rom 29:78-83, 1991; of record) as applied to claims 37, 39, 41, 43, 44, 46 and 55 above and further in view of Halpern et al (Infection and Immunity 58(4):1004-1009, 1990; of record).

Wilson et al (Vaccine, 11(2):113-118, 1993) and Nenconi et al (Acta Med Rom 29:78-83, 1991) are combined as set forth supra. The references as combined do not teach tetanus toxin C-fragment.

Halpern et al teach that tetanus toxin Fragment C can be a suitable alternative to tetanus toxin in many applications (see abstract). Halpern et al also teach that the C fragment antigen retains the activity of the intact tetanus toxin avoiding the need to use the intact tetanus toxin which requires toxioding.

It would have *been prima* facie obvious to one having ordinary skill in the art at the time that the invention was made to substitute the tetanus C-fragment for the tetanus toxoid in the method of Wilson and Nenconi et al as combined *supra* because Halpern et al teaches is a suitable alternative for tetanus toxin in many applications and that the tetanus C fragment avoids the need to use the intact tetanus toxin which requires toxoiding and therefore would have the benefit of reducing the processing time of the antigens for the vaccine.

Status of Claims

Claims 37, 39, 41-46 and 55 stand rejected. Claims 47-54 are withdrawn from consideration as drawn to a non-elected invention.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-F 6:30 pm - 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patricia A. Duffy, Ph.D.
Primary Examiner
Art Unit 1645